Summary of Health Data for

SUMMARY

was tested for oral, dermal, and inhalation acute toxicity; skin and eye irritation; skin corrosion; and mutagenicity. The material has an acute oral LD_{50} of 2295 mg/kg, an acute dermal LD_{50} of >2000 mg/kg, and an acute aerosol inhalation LC_{50} (4 hr exposure) of between 1.49 and 2.44 mg/L. The material was severely irritating to eyes, moderately irritating to skin, and not corrosive to skin of rabbits. The material was not mutagenic in the *in vitro* Ames assay.

TOXICOLOGY DATA

Acute Toxicity

Oral. An acute oral toxicity study was performed by administering the undiluted test substance to 10 (5 male / 5 female) albino Sprague-Dawley rats via oral gavage at a dose concentration of 5000 mg/kg. All animals receiving this concentration died, therefore additional concentrations were tested. Acute oral toxicity was determined by administering the undiluted test substance to 4 groups of 10 (5 male / 5 female) albino Sprague-Dawley rats via oral gavage at doses of 0, 500, 1200, and 3000 mg/kg. Animals were observed daily for 14 days for mortality and morbidity. Surviving animals were sacrificed and all animals were examined macroscopically. Four male and all 5 female animals receiving 3000 mg/kg concentration dose died during the study. There were no deaths among rats receiving 500 or 1200 mg/kg. The acute oral LD_{50} was calculated to be 2295 mg/kg for male and female animals combined. Clinical signs of reaction to treatment included piloerection (among rats at all dosages), hunched posture, unsteady gait, pallid extremities, eyes dulled, increased salivation, abnormal respiration, ungroomed appearance, fecal disturbances, increased sensitivity, and increased lacrimation (among rats at 1200, 3000, and/or 5000 mg/kg), walking on toes, blue/cold extremities, lethargy, partially closed eyelids, and body tremors (among rats at 3000 and 5000 mg/kg) and prostration (5000 mg/kg only). Resolution of clinical signs was complete in all surviving animals by day 6. Macroscopic pathology of animals that had died during the study revealed congestive changes in the majority of organs and tissues. There were no abnormalities observed among animals sacrificed at study termination (2).

Dermal. A study was conducted to determine the acute dermal toxicity of the test substance by administering at a dose level of 2000 mg/kg to the clipped dorso-lumbar region of 10 (5 male/5 female) New Zealand White rabbits for 24 hours. Treatment areas were covered with gauze, non-irritating dressing, and waterproof dressing. At the end of the exposure period, dressing was removed and the skin washed. All animals were observed twice daily for mortality and

morbidity for 14 days. Animals were examined for dermal response once daily throughout the 14-day observation period. No deaths occurred during the study. The acute dermal LD_{50} was determined to be >2000 mg/kg. With the exception of fecal disturbance (few feces) in one female rabbit on day 3, there was no evidence of systemic response to treatment in any animal during the study. Persistent slight to moderate irritation was evident in all animals. Irritation had resolved by the second week of observation for all but 3 animals for which slight erythema was still evident at study termination. (6).

Skin Irritation. A skin irritation study was conducted by administering undiluted test substance at a dose of 0.5 ml to one intact skin site on the clipped dorso-lumbar region of each of 3 female New Zealand White rabbits. Semi-occlusive dressings were used and the exposures lasted 4 hours. At the end of the exposure period, the dressings were removed and skin was washed with warm water to remove any residual test substance. Animals were observed twice daily for mortality and morbidity for 14 days. Animals were scored for irritation at 56 minutes, 24, 48, and 72 hours following removal of the dressings. Additional observations were made on days 5-10 for all animals, day 11 for 2 animals, and on days 12-14 for one animal. There was no evidence of systemic response to treatment. The exposure to the test substance elicited well-defined erythema in all three animals and was accompanied in one by very slight edema. Desquamation of the stratum corneum developed in all animals. Dermal reactions had completely resolved in all animals by day 10, 11, or 13. The Primary Irritation Index (PII) was calculated to be 2.11 (3).

Skin Corrosion. The test substance was tested to determine its skin corrosion potential. Only slight redness was observed in all test animals and slight swelling observed at the application site with two of the six rabbits following a four-hour exposure to the test material. Very slight redness was noted after 48 hours but no evidence of necrosis was observed at any reading interval. These data indicate this material was not corrosive to the skin of rabbits (1).

Eye Irritation. An eye irritation study was conducted by administering a dose of 0.1 ml undiluted test substance to one eye of each of three female New Zealand White rabbits. Each animal's untreated eye served as a negative control. Animals were observed twice daily for mortality and morbidity. Ocular response was determined at 1 hour and at 1, 2, and 3 days after exposure. Additional observations were collected for all animals 4, 7, 14, and 21 days after instillation. No deaths occurred during the study and there were no signs of systemic reaction to the exposure. A single instillation of test substance into the eye of the rabbit elicited dulling of the cornea developing into corneal opacification in one animal, corneal opacification in two animals and vascularization on the cornea in all three animals. Iridial inflammation, a diffuse beefy red coloration of the conjunctivae, swelling of the lids about half-closed, discharge with moistening of the lids and hairs and considerable area around the eyes was seen in all three animals. Corneal opacification persisted in two animals and hyperemia of the blood vessels on

the conjunctiva with or without slight swelling in all three animals at study termination (day 21). As a result of the ocular reactions observed, the test substance was classified as a severe eye irritant (4).

Inhalation. The acute aerosol inhalation toxicity of the test material was evaluated using 6 groups of 10 (5 male/5 female) Sprague-Dawley rats, exposed for 4 hours via whole-body exposure to an aerosol generated from the test substance at the following concentrations: 0, 0.515, 1.06, 1.49, 2.44, or 5.75 mg/L. The mass median aerodynamic diameter (MMDD) of >96% of particles was <7 um (respirable to the rat). Rats were observed continuously for signs of reaction to the test substance during exposure and twice daily for a 14-day observation period. Surviving animals were sacrificed after the observation period and all animals were observed for macroscopic effects. All 5 male and 4 female animals from the highest concentration group (5.75 mg/L) died during exposure or by day 3 of the observation period. All 5 males and 3 females from the 2.44 mg/L concentration group died during exposure or by day 2 of the observation period. All animals in the 1.49 mg/L, 1.06 mg/L, 0.515 and the control group survived. The acute aerosol LC_{50} for the test substance was determined to be between 1.49 and 2.44 mg/L. Clinical signs observed during exposure included exaggerated breathing and eyes partly closed (in all test groups), and reduced motor activity (0.515 – 2.44 mg/L groups). Clinical signs presented during the observation period included irregular, noisy and/or exaggerated breathing (in all test groups), partially closed eyes (1.06, 1.49, 2.44, and 5.75 mg/L groups), lethargy (2.44 and 5.75 mg/L groups), and ataxia (5.75 mg/L group only). A dose related reduction in body weight gain over the observation period was seen in animals from the 1.49, 2.44, and 5.75 mg/L groups. Severely congested lungs were seen in all decedent animals. Areas of severe congestion together with pale raised hardened areas were seen in the lungs of the animal surviving the 5.75 mg/L exposure. Surviving female rats exposed to 5.75 or 2.44 mg/L had lung weights greater than control rats. In all other surviving animals from other test groups, there were no differences in organ weights that were considered to be a direct effect of exposure to the test aerosol (5).

Genetic Toxicity

In Vitro. The test material was evaluated for genotoxicity in the Ames reverse mutation assay using *Salmonella typhimurium* (TA1535, TA1537, TA98, and TA100 strains) and *Escherichia coli* (WP2 strains). Bacteria were exposed to dose levels of 50, 150, 500, 1500, and 5000 µg/plate of the test substance (diluted in water) in the presence and absence of a mammalian activation system (S9). No evidence of mutagenic activity was seen at any dose level in either bacterium, with or without activation (7).

REFERENCES

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